

REMARKS

Claims 1-4, 6, 20-34, 42, 46-48, and 77-82 are pending. Applicant amends claims 1, 20-22, 29, 31-34, 42, 46, and 47-48. Applicant adds new claims 84-88. No new matter is added, as shown by the specification support for each claim below:

CLAIM	RECITATION	SPECIFICATION
84	the excitable cells comprise hypertrophic cardiac myocytes	Page 46, lines 14-19
85	the cross sectional area of hypertrophic cardiac myocytes is reduced	Page 47, lines 5-16
86	one or more indices of systolic function of the hypertrophic heart are altered	Page 47, lines 18-47
87	pre-load independent contractility $((dp/dt_{max})/EDV)$ is reduced	Figure 9A-9B, Figure 6
88	fibrosis of the hypertrophic heart is reduced	Page 16, lines 7-9

Claim Rejections Under 35 U.S.C. § 112, first paragraph

Enablement

While the Patent and Trademark Office has recognized that the amendments made in the previously filed response addressed some of the Patent and Trademark Office's concerns regarding the unpredictability of any nucleic acids encoding the GEM protein (Office Action, pages 3-4), claims 1-4, 6, 20-34, 42, 46-48, and 77-82 remain rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. The Patent and Trademark Office indicates that the method is unpredictable across the full scope of the claims. In particular, the U.S. Patent and Trademark Office asserts that the portions of the claims that reads on the use of naked DNA and on undefined variants of GEM protein are not enabled.

In order to expedite prosecution, applicant amends independent claims 1 and 46 to recite methods for modulating calcium channel activity in which:

- a recombinant adenovirus is used; and
- the adenovirus comprises a nucleic acid encoding a GEM protein having an amino acid sequence according to SEQ ID NO.: 1.

As recognized by the Patent and Trademark Office, adenovirus delivery yields only 15-25% transduction of excitable cells (Office Action, page 4). Miaki teaches that this transduction efficiency, is non-lethal. (Miaki, J. et al., *J. Clin. Invest.*, Vol. 111:1529-1536 (2003)). Moreover, the specification provides sufficient information to practice the claimed invention without undue experimentation. For example, in Example 1 and on page 49, lines 1-6, the specification provides enabling disclosures (*e.g.*, dose, route, methods, etc.) relating to the delivery of adenovirus vector that results in non-lethal levels of cellular GEM expression.

In addition, applicant amends independent claim 47 to recite a method for attenuating cardiac hypertrophy by modulating the activity of a calcium channel in a predetermined region of excitable cells in a mammal using:

- a nucleic acid encoding a variant of a GEM protein having an amino acid sequence according to SEQ ID NO.: 1 comprising an amino acid substitution of glycine for tryptophan at position 269 of SEQ ID NO.: 1;
- to treat a heart afflicted with hypertrophy due to cardiac damage or disease
- resulting in attenuation of the cardiac hypertrophy.

Amended independent claim 47 specifically recites the contacting of hypertrophic cells with the W269G GEM mutant, which as disclosed in Example 4 and Figure 5 of the specification, consistently attenuates indicia of cardiac hypertrophy. In order to further define the aspects of cardiac hypertrophy that are affected by the W269G GEM variant, applicant has added new claims 84-88.¹ Moreover, the data disclosed in the specification demonstrates the consistent effect of the W269G GEM variant on cardiac hypertrophy, thereby addressing the Patent and Trademark Office's concerns regarding the alleged unpredictability of using the W269G variant.

In view of the amendments and remarks above, applicant respectfully submits that independent claims 1, 46, and 47, and their respective dependent claims, are fully enabled by the specification as filed. Please withdraw the rejections under 35 U.S.C. § 112, first paragraph for lack of enablement.

Written Description

¹ These are supported at least at pages 47-48 and in the drawings. See table above. Thus, no new matter is presented by these amendments.

Claims 1-4, 6, 20-34, 42, 46-48, and 77-82 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. The Patent and Trademark Office asserts that applicant was not in possession of additional variants of the GEM protein beyond the W269G variant. Applicant has amended the claims to remove reference to GEM variants other than the wild-type or the W269G variant. Please withdraw the written description rejections under 35 U.S.C. § 112, first paragraph.

Claim Rejections Under 35 U.S.C. § 112, second paragraph

The Patent and Trademark Office rejected claims 2-4, 6, and 20-31 under 35 U.S.C. § 112, second paragraph as being indefinite due to improper dependent claim format.² Applicant inadvertently filed a response with typographical errors in the claim dependencies.³ Applicants thank the Patent and Trademark Office for interpreting the dependencies in a manner which permitted examination. The present claim set has been corrected to use proper dependencies.⁴ Please withdraw the rejections under 35 U.S.C. § 112, first paragraph.

Applicants have addressed and overcome the rejections under 35 U.S.C. § 112, first and second paragraphs. Please withdraw the rejections. All claims are in condition for allowance.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, applicant does not concede that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter that may in the future be found to be specifically disclaimed herein or in any prior applications or amendments. Accordingly, reviewers of this or any parent, child or related

² Applicants did not intend to amend the claims but inadvertently listed a “claim 0” rather than “claim 1.”

³ On September 7, 2009

⁴ as existed in the claim set of December 15, 2009

prosecution history cannot reasonably infer that applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

Co-Pending Applications of Assignee

Applicant draws the Examiner's attention to the following co-pending applications of the present application's assignee:.

Attorney Docket No.	App. No.	Filing Date	Title
439	10092184	03/05/2002	Gene Delivery Compositions and Methods
441	09947953	09/06/2001	Cardiac Arrhythmia Treatment Methods
449	9977865	10/15/2001	Methods and Compositions for Nucleic Acid Delivery
454	10476259	10/27/2003	Biological Pacemaker
459	10678723	10/02/2003	Focal Calcium Channel Modulation
464	60062018	10/10/1997	Gene Delivery Compositions and Methods
465	9169739	10/08/1998	Gene Delivery Compositions and Methods
471	10855989	05/28/2004	Cardiac Arrhythmia Treatment Methods
472	10855892	05/28/2004	Cardiac Arrhythmia Treatment Methods
473	10855805	05/28/2004	Cardiac Arrhythmia Treatment Methods
516	11007315	10/09/2004	Gene Delivery Compositions and Methods
610	11508957	08/24/2006	Cardiac Arrhythmia Treatment Methods
671	11905757	10/03/2007	Focal Calcium Channel Modulation
690	12034077	02/21/2008	Cardiac Arrhythmia Treatment Methods and Biological Pacemaker
696	12089460	04/07/2008	Biologically Excitable Cells
83648	9407945	09/29/1999	Induced Genetic Suppression of Cellular Excitability

Respectfully submitted,
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